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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,627	07/06/2001	Charles David Weaver	3035-4086US1	7563

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/900,627	WEAVER ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31 and 121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-26, 28-31* is/are rejected.

7)☒ Claim(s) *6,7,27 and 121* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 1/26/2007 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 32-120 are cancelled.
2. Claim 121 is added to the instant application.
3. Claims 1-31 and 121 are under examination.

Claim Objections

1. Claim 1 is objected to because of the following informalities: line 6, ""contact the cells" should be "capable of contacting the cells" because the claim directs to an apparatus, the cells are not contacted yet. Appropriate correction is required.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1-4, 12-13, 20-26 are rejected under 35 U.S.C. 102(e) as being anticipated by Rava et al. (US 20050282156).

Rava et al. teach an apparatus for biological throughput analysis. The apparatus comprises a cell support membrane component for supporting one or more cells which comprises a first layer (see Figure 5; component 560, microtiter wells) comprising a non-conductive material comprising a top surface and bottom surface where a pore (microtiter

through hole) extending between, through, said top and bottom surfaces. This first microtiter layer *allows* cell attachment and forming electrically tight seals with the contacted cells at the cell attachment sites (See Figure 5; Note, the apparatus is suitable for analysis a variety of analytes, including receptors, antibody, nucleic acid, cells, cell membrane- See Section 0026). The top surface of microtiter well layer, e.g. a substrate capable of letting cells for attachment where the cell attachment sites circumscribe the microtiter wells and the wells are spaced that it is capable of contact one cell for one well. Note, there is no definition in the specification as to what constitutes "cell attachment sites". Examiner takes the position that any suitable substrate is capable for cell attachment, e.g. top surface, inside the microtiter wells, microtiter walls, are all capable for cell attachment. Underneath the first microtitier well layer, a second layer (component 520 in Figure 5) comprises a non-conductive materials which directly contacts the first layer and spans across at least one pore (microtiter well) (See Figure 5). With respect to the intended use, i.e. measuring electrical conditions, the apparatus taught by Rava et al. is also capable of this function, e.g. placing target cells in the first layer microtiter wells and measuring electrical potential change by inserting electrodes (Note, the claim language is an open transition "comprising"). Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. measuring cellular electrical conditions, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

With respect to claims 3-4, Rava et al. teach the materials for the layers, including polypropylene, polystyrene, polycarbonate (See Section 0060; 0064).

With respect to claim 12-13, there are at least 96 pores in the first layer (See Figure 3 and Figure 4).

With respect to claims 20-26, the features "the area of the second layer of the cell support membrane component is *removable*" from the instant invention is inherently obtainable by the recited device. The case law has established that the production of a product by a particular process does not impart novelty or unobviousnes to a product when the same product is taught by the prior art-"[Where] the claimed and prior art products are identical or substantially identical in *structure or composition*, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)(emphasis added). This is particularly true when the properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art. See In re Kind, 207 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F.2d 599, 601, 38 USPQ 143, 144-145 (CCPA 1938); In re Bergy, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979). The second layer of the Rava's apparatus, component 520 in Figure 5, can be removed by photo-ablation assisted by confocal microscope.

3. Claims 1-2, 12-13, 15, 18-19, 20-26, 28-29 are rejected under 35 U.S.C. 102(e) as being anticipated by McDevitt et al. (US 6649403).

McDevitt et al. teach a microarray apparatus for screening multiple biological samples. The apparatus comprises a cell support membrane component for supporting one or more cells which comprises a first layer (see Figure 2; component 210) comprising a non-conductive material comprising a top surface and bottom surface where a pore extending between, through, said top and bottom surfaces. The surface this first layer allows cell

attachment and forming electrically tight seals with the contacted cells at the cell attachment sites (See Figure 2 and 3; Note, the apparatus is suitable for analysis a variety of analytes, including bacteria See Col. 6, line 17-25). Underneath the first layer, a second layer (component 220) comprises a non-conductive material which directly contacts the first layer and spans across at least one pore (See Figure 2). With respect to the intended use, i.e. measuring electrical conditions, the apparatus taught by McDevitt et al. is also capable of this function, e.g. placing target cells in the first layer cavity wells and measuring electrical potential change by inserting electrodes (Note, the claim language is an open transition "comprising"). Applicant is reminded that a recitation of the intended use of the claimed invention, i.e. measuring cellular electrical conditions, must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963).

With respect to claims 12-13, there are more than 4 pores in the first layer (See Figure 3).

With respect to claims 15 and 18, McDevitt et al. teach that the apparatus can also use to study neuron cells which inherently expresses ion channel, such as sodium, potassium or calcium ions (See Figure 49, Col. 64, line 5-20).

With respect to claim 19, McDevitt et al. teach using Triton-X detergent to enhance the affinity of cellular receptor for analyte, which is capable of permeabilizing cells (Col. 63, line 34-38).

With respect to claims 20-26, the features "the area of the second layer of the cell support membrane component is *removable*" from the instant invention is inherently obtainable by the recited device as discussed above.

With respect to claims 28-29, McDevitt et al. teach placing the apparatus in a chamber (component 550 in Figure 17) which includes a top and a bottom area where the cell attachment sites from the apparatus facing the top area of the chamber (See Figure 17). For the apparatus, electrolye solution, e.g. buffer, are placed within the pores (cavities) for analysis.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rava et al. in view of Marra et al. (US 6165486).

Rava et al. reference has been discussed but is silent in teaching using a material recited as in claim 5.

Marra et al. teach using a substrate containing polycaprolactone would be better for the growth of cell (Col. 10, line 38-45).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Rava et al. with the polycaprolactone substrate as one the second layer as taught by Marra et al. for better cell growth. One ordinary skill in the art would have been motivated to do so in order to for better results on cellular experiments/or detection.

7. Claims 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rava, or McDevitt et al. in view of Baumann et al. (US 6475760).

Both Rava or McDevitt et al. references have been discussed but are silent in teaching treating cell support with poly-L-lysine for facilitation of cell attachment.

Baumann et al. teach using fibronectin, poly-L-lysine for facilitation of cell attachment for measuring cellular electrophysiological potential (Col. 3, line 30-32; Col. 6, line 27-37).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Rava or McDevitt et al. with the poly-L-Lysine as taught by Baumann et al. on the cell support of the apparatus in order to increase cell attachment for better efficiency for further cellular analysis. One ordinary skill in the art would have been motivated to do so because cell attachment is important for measuring cell electrical potential, and increasing attachments would provide better results and efficiency of the experiments.

8. Claim 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rava or McDevitt et al. in view of Bossuyt et al. (US 6585969).

Rava or McDevitt et al. references have been discussed but do not explicitly teach using materials, such as silicone or Teflon, to inhibit cell attachment.

Bossuyt et al. teach treating the cell culture vessel with silicone will make the walls sufficiently hydrophobic to prevent cell adhesion to increase specificity for cell culturing (Col. 14, last paragraph to Col. 15, line 1-2).

Therefore, it would have been obvious to have motivated one skilled in the art at the time when invention was made to have provided Rava or McDevitt et al. to apply the treatment of silicone to the outside of the cell attachment site as taught by Bossuyt et al. to further increase cell attachment to the target area while preventing non-target cells binding because silicone treatment to the outside of the cell attachment site can prevent cell from adhesion outside of the electrical measurement area and cause more specific and efficient cell attachment to the electrical measurement area. One artisan in the field would have been motivated to do so for more efficiency and better specificity.

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over McDevitt et al..

McDevitt et al. reference does not explicitly disclose particular diameter range for the pores. However, McDevitt et al. disclose that the biological particles used for detection having diameter range from 0.05 –500 microns (Col. 11, line 13-16).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to chose appropriate size microarray well since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over McDevitt et al. in view of Bukoski et al. (US 6184254).

McDevitt et al. teach using the apparatus to study neuron cells, but fail to disclose a specific neuron cell for study..

Bukoski et al. disclose study the dorsal root ganglia for neuron physiology and observed existing calcium +2 receptor (See Example 4 and 7).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided McDevitt et al. with a specific neuron cells, such as dorsal root ganglia as taught by Bukoski et al. because the dorsal root ganglia have been shown involving import neuron Ca+2 receptor and one ordinary skill in the art would have been motivated further analyzing these cells for more cellular electrophysiology study.

11. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over McDevitt et al. in view of Smith et al. (US 6448469).

McDevitt et al. teach using the apparatus to study neuron cells, but fail to disclose use of cells having construct containing ion channel proteins.

Smith et al. teach using genetic recombinant DNA construct to produce membrane proteins for cell biology study. Smith et al. teach using DNA construct containing a membrane ion channel protein to produce such proteins (See claim 24 and 26).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided McDevitt et al. with a ion channel protein produced by a cell containing membrane ion channel protein as taught by Smith et al.. Using molecular recombinant technique for producing a specific protein is well-known and merely involves routine skill in the art. Ion-channel proteins are located on the neuron cells, and one ordcnary skill in the cellular electrophysiology art would have been

motivated to study the ion channel proteins for further understanding the cellular mechanism.

12. Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over McDevitt et al. with Owen et al. (WO 9966329).

McDevitt et al. teach using the apparatus to study neuron cellular activity in a chamber but is silent in using two electrodes for voltage-clamp on the cells.

Owen et al. teach an appratus measuring neuron cellular membrane potential. Owen et al. teach placing two electrodes in a chamber one electrode facing the top surface of the first layer on the cell support, and the other electrode facing the bottom surface of the support (See Figure 1-2).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided McDevitt et al. with the two electrodes as taught by Owen et al. for measuring the cellular potential. One ordinary skill in the art would have been motivated to do so because both references are in analogous art, e.g. neuron study, and measuring membrane potential, e.g. voltage-clamp, from neuron cells is widely practiced in the neuron science field, and ordinary artisan like McDeviit et al. would have been motivated to use the same methodology to measure the cellular potential.

Response to Applicant's Arguments

13. Applicant's arguments with respect to claims 1-31 have been considered but are moot in view of the new ground(s) of rejection.

14. The rejections based on Meyer et al. reference have been withdrawn because Meyer et al. do not disclose a layer (first layer) which has through holes from the top surface to the bottom

surface. Meyer et al. teach using micro-curvette for the first layer. The micro-curvette also receive cells which cannot be "through".

Allowable Subject Matter

15. Claims 6-7, 27 and 121, are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. The following is a statement of reasons for the indication of allowable subject matter: no prior art teaches or fairly suggests an apparatus having two layers where the second layer contacted the first layer having cell attachment is selectively removed by enzyme where the second layer contains a dye for enhancement of absorbing laser energy for better ablation. The prior art teaches using two layers apparatus for cellular analysis, such as Rava et al. or McDeviit et al., however, the second layers from both references are necessary substrates for holding cells, and the materials used for this layer are not biodegradable and cannot be digested by enzymes.

Conclusion

17. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jacob Cheu
Examiner
Art Unit 1641

April 13, 2007